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10/535,270	02/09/2006	Rex W. Newkirk	101927/43	5756

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EXAMINER	
MI, QIUWEN	
ART UNIT	PAPER NUMBER
1655	

NOTIFICATION DATE	DELIVERY MODE
08/19/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/535,270	NEWKIRK ET AL.	
	Examiner	Art Unit	
	QIUWEN MI	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 May 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment in the reply filed on 8/5/09 is acknowledged. Claims 1-20 are pending. **Claims 1-20 are examined on the merits.**

Any rejection that is not reiterated is hereby withdrawn.

Claim Rejections –35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-20 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Siren (US 4,734,283), in view of Siren (US 4,797,390), further in view of Vanderbeke et al (US 5,554,399).

This rejection is maintained for reasons of record set forth in the Office Action mailed out on 2/10/09, repeated below. Applicants' arguments filed have been fully considered but they are not deemed to be persuasive.

Siren (US 4,734,283) teaches ground beans, 100 g, containing 1% myo-inositol-hexaphosphate (thus a phytic acid) were suspended in 1000 ml sodiumacetate buffer at pH 5.2. 500 mg crude wheat phytase (thus a phytase enzyme, thus the phytase enzyme does not include acid phosphatase) (from Sigma Chemical Co) was added. The mixture was incubated at 55.degree. C. at shaking. After an incubation period of 12 hrs the slurry (thus an aqueous slurry

of plant material) was frozen to -10.degree. C. in order to stop the hydrolysis. 10 g of the frozen material was extracted with 100 ml 0.4M HCl. The suspension was shaken for 1 hour and subsequently centrifuged. The supernatant was collected (thus separating said slurry into a water soluble fraction and a water-insoluble fraction) and neutralized to pH 7 with an aqueous solution of NaOH. A sample of the supernatant was analyzed with HPLC. The IP_3 content of the extract was 40 mg IP_3 (col 15, Example 22) (thus negatively charged, thus a partial hydrolysis). Siren (US 4,734,283) further teaches another example: a 1.6 gram quantity of sodium phytate (from corn, Sigma Chemical Co) was dissolved in 650 ml sodium acetate buffer, pH 5.2. 2.7 gram wheat phytase (thus a phytase enzyme) (EC 3.1.3.26, 0.015 U/mg, from Sigma Chemical Co) was added and the mixture was incubated at 38.degree. C. The dephosphorylation was followed by determining the inorganic phosphorus released. After 3 hours when 50% inorganic phosphorus was liberated the hydrolysis was stopped by adding 30 ml ammonia to pH 12. A liquid mixture containing inositolphosphates (thus negatively charged) was obtained. 350 ml of the mixture was passed through an ion-exchange column (Dowex 1, chloride form, 25 mm.times.250 mm) and eluted with a linear gradient of hydrochloric acid (0-0.7N HCl). Aliquots of eluted fractions were completely hydrolyzed (thus hydrolyzing the inositol phosphates in said first ionic fraction) in order to determine the contents of phosphorus and inositol. The peaks correspond to different inositolphosphates (thus a partial hydrolysis) i.e. a peak with the ratio of phosphorus to inositol of three to one consists of inositoltriphosphate etc. Two fractions with the ratio of phosphorus to inositol of three to one were obtained (thus separating the hydrolyzed first ionic fraction into a second ionic fraction and a second neutral fraction which contains purified inositol) (col 16, Example 25).

Siren (US 4,734,283) does not teach the phytase enzyme includes acid phosphatase, the hydrolysis carried out at a pH of less than 4, separating the slurry into a water-soluble fraction and an insoluble fraction carried out by filtration, or hydrolyze inositol phosphates in first ionic fraction with acid phosphatease or phytase.

Siren (US 4,797,390) teaches that according to the invention a procedure where the above mentioned higher inositol phosphate IP.sub.6, IP.sub.5 and/or IP.sub.4 are broken down enzymatically to IP.sub.3 with phytase enzyme, for instance, is preferred. Phytase enzyme is normally present in all inositol phosphate containing plants and seeds. Because of this it is, according to the invention, usually not necessary to add the enzyme if a natural product is used as starting material. In the cases where the natural product has too low an enzymatic activity or when IP.sub.6, IP.sub.5 or IP.sub.4 or a mixture of these is used as starting material, a phytase enzyme, for example, from bran is added (page 4, lines 25-38). Siren (US 4,797,390) also teaches the content of the peak with the ratio of phosphorus to inositol of six to one was precipitated by addition of calciumhydroxide. The precipitate was filtered, washed and mixed with 10 ml of a cation-exchange resin to give the acid form of the inositolhexaphosphate. After neutralization with sodium hydroxide and freeze-drying the sodium salt of D-chiro-inositolhexaphosphate was obtained.

Vanderbeke et al teach an enzyme composition having a synergetic phytate hydrolyzing activity comprising a phytase having phytate hydrolyzing activity at a pH of from 2.5 to 5.0 and an acid phosphatase having phytate hydrolyzing activity at a pH of 2.5, in a low ratio corresponding to a pH 2.5/5.0 activity profile of from 0.8/1.0 to 3/1. Said enzyme composition preferably displays a higher synergetic phytate hydrolyzing efficiency through thermal treatment

(see Abstract). Vanderbeke et al also teach by using a mixture of acid phosphatase and phytase instead of phytase as sole enzyme, plant phytin hydrolysis is improved, not solely as a result of a higher thermostability of this enzyme mixture, but mainly as a result of an improved synergetic interaction between both enzymes as the ratio pH 2.5/5.0 phytate hydrolyzing activity will increase by the different thermal degradation of both enzymes (col 5, lines 60-67). Vanderbeke et al further teach most preferably the treatment is carried out at a pH of about 2.5 (thus less than 4).

It would have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to either use the phytase enzyme that is normally present in all inositol phosphate containing plants and seeds to hydrolyze the inositol phosphates in the first ionic fraction, or newly add a phytase enzyme to hydrolyze the inositol phosphates from Siren (US 4,797,390) since Siren (US 4,797,390) teaches higher inositol phosphate IP.sub.6, IP.sub.5 and/or IP.sub.4 are broken down enzymatically to IP.sub.3 with phytase enzyme either naturally contained in the plants and seeds or freshly added when the enzyme level is low. It would also have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to use filtration to separate the slurry into a water-soluble fraction and an insoluble fraction as evidenced by Siren (US 4,797,390), filtration is a routine operation that is used in phytate hydrolyzation process.

It would also have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to include acid phosphatase with phatase from Vanderbeke et al to hydrolyze phytate, phytic acid, phytin or inositol phosphates since Vanderbeke et al teach the enzyme composition displays a higher synergetic phytate hydrolyzing efficiency. It would also

have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to treat the aqueous slurry at pH less than 4, since Vanderbeke et al teach preferably the treatment is carried out at a pH of about 2.5.

Since all the references yielded beneficial results in hydrolyzing phytate in plant materials, one of ordinary skill in the art would have been motivated to make the modifications to combine the references together.

From the teachings of the references, it is apparent that one of the ordinary skills in the art would have had a reasonable expectation of success in producing the claimed invention.

Thus, the invention as a whole is *prima facie* obvious over the references, especially in the absence of evidence to the contrary.

Applicant argues that "Siren 1 and Siren 2 essentially teach the production of inositol phosphate intermediates Siren 1 teaches partial hydrolysis of IP6 with phytases to obtain the desired IP3 isomer, and adding IP3 to a food composition in an amount sufficient to provide a final concentration of 5 mg of IP3 per 100 g of food composition. The hydrolysis is carried out at a temperature of 20-70° C and a pH of 4 to 8. The hydrolysis is stopped when the liberation of about 30%-60% of the total ester phosphorous has been achieved. A food composition is then made wherein a source of IP3 is added to the composition such that the desired amount mentioned above is achieved. Siren 1 does not teach the novel and inventive elements of the present invention, namely separating the slurry into a water soluble fraction and an insoluble fraction, separating the water soluble fraction into a first ionic fraction containing anionic components comprising inositol phosphates and a

further other fraction which contain neutral fractions; hydrolyzing the inositol phosphates in said first ionic fraction; and separating the hydrolyzed first ionic fraction into a second fraction and a second neutral fraction which contains inositol (page 6, last paragraph bridging page 7).

This is not found persuasive. Siren (US 4,734,283) teaches ground beans, 100 g, containing 1% myo-inositol-hexaphosphate (thus a phytic acid) were suspended in 1000 ml sodiumacetate buffer at pH 5.2. 500 mg crude wheat phytase (thus a phytase enzyme, thus the phytase enzyme does not include acid phosphatase) (from Sigma Chemical Co) was added. The mixture was incubated at 55.degree. C. at shaking. After an incubation period of 12 hrs the slurry (thus an aqueous slurry of plant material) was frozen to -10.degree. C. in order to stop the hydrolysis. 10 g of the frozen material was extracted with 100 ml 0.4M HCl. The suspension was shaken for 1 hour and subsequently centrifuged. The supernatant was collected. Thus Siren 1 teaches separating said slurry into a water soluble fraction and a water-insoluble fraction. Siren 1 teaches aliquots of eluted fractions were completely hydrolyzed, thus Siren 1 teaches hydrolyzing the inositol phosphates in said first ionic fraction, in order to determine the contents of phosphorus and inositol. Siren 1 teaches the peaks correspond to different inositolphosphates (thus a partial hydrolysis) i.e. a peak with the ratio of phosphorus to inositol of three to one consists of inositoltriphosphate etc. Two fractions with the ratio of phosphorus to inositol of three to one were obtained. Thus Siren 1 teaches separating the hydrolyzed first ionic fraction into a second ionic fraction and a second neutral fraction which contains purified inositol.

Applicant argues that “Siren 2 teaches a process where the higher inositol phosphates are broken down enzymatically to IP3 with phytase enzyme and then added to a pharmaceutical

composition in an amount sufficient to reduce the negative effect of cadmium or aluminum in the body. The enzyme is allowed to act for as long a time as is necessary for the degree of partial hydrolysis to be achieved. Siren 2 does not teach what is missing from Siren 1. Column 4, lines 25-38 of Siren 2 referenced by the Examiner merely teaches adding phytase enzyme where the starting material has too low an enzymatic activity to break down higher inositol phosphates to IP3. Siren 2 mentions ion exchange, however this is in the context of isolating or fractionating the various inositoltriphosphate isomers, and not for separating negatively charged inositol phosphates from the other neutral components. Siren 2 does not teach using hydrolysis to manipulate the charge characteristics of the mixture or how to isolate neutral inositol from other neutral sugars in solution such as fructose, glucose and sucrose that are present at high concentrations in a slurry of plant material (page 7, last paragraph).

This is not found persuasive. Siren 2 was brought in because Siren 2 teaches using the phytase enzyme that is normally present in all inositol phosphate containing plants and seeds to hydrolyze the inositol phosphates in the first ionic fraction, or newly add a phytase enzyme to hydrolyze the inositol. Siren 2 also teaches using filtration to separate the slurry into a water-soluble fraction and an insoluble fraction.

Applicant argues that "The core of the present invention is to utilize a method for the partial hydrolysis of phytate to charge intermediates, separate these negatively charged intermediates from the neutral sugars in solution and then complete the full hydrolysis to neutral inositol that can be readily separated from charged ions and compounds using known charged based separation techniques. The elements of claim 1 and dependent claims 2-20 are not taught

by Siren 1 or Siren 2 individually, nor by the combination of Siren 1 and Siren 2" (page 8, 1st paragraph).

This is not found persuasive. As mentioned above, Siren 1 and 2 teach the core invention as indicated above.

Applicant argues that "Vanderbeke teaches an enzyme composition having a synergetic phytate hydrolyzing activity comprising a phytase having phytate hydrolyzing activity at a pH of 2.5 to 5.0 and an acid phosphatase having phytate hydrolyzing activity at a pH of 2.5. The invention provides a process for hydrolyzing phytate, comprising the step of treating a raw material which contains phytate with the synergetic enzyme composition, said treatment being carried out under hydrolyzing conditions at a pH where the phytase and acid phosphatase of said enzyme composition have hydrolyzing activity" (page 8, 2nd paragraph). Applicant also argues that "This is completely different from the partial hydrolysis in step 1 (a) of the present invention which is preferably carried out in the absence of acid phosphatase, and to the extent that acid phosphatase is present, the pH is adjusted to be above 2.5 and more specifically between 3 and 7 in order to avoid hydrolysis to free inositol by acid phosphatase. According to the present invention the inositol phosphates contain negatively charged phosphate intermediate groups on the inositol ring after partial hydrolysis in step l(a). As such the inositol phosphate intermediates products of partial phytate hydrolysis are charged and are in solution along with neutral sugars such as glucose, fructose and sucrose. The charged state of the inositol phosphates allows for ease of separation from neutral sugars in solution using separation techniques that are based on the physical property of electrical charge of the components of the solution. After the charged based separation is complete, the ionic fraction

containing the inositol phosphates and other charged ions and molecules is subjected to full hydrolysis of the inositol phosphates in step (d) to yield inositol plus inorganic phosphate. The result is the formation of the neutral sugar inositol in a fraction containing charged compounds and ions. The neutral inositol compound can then be separated in a pure form from the charged components of the solution using the same charged based separation techniques" (page 8, last paragraph bridging page 9). Applicant further argues that "Vanderbeke does not teach the step of slurrying the plant material, partial hydrolysis of phytate with the goal of generating charged inositol phosphate intermediates, separating the soluble fraction from the insoluble fraction, charge based separation, followed by full hydrolysis of the inositol phosphates, and separating the inositol from the ionic fraction. The synergetic enzyme composition and its synergetic phytate hydrolyzing activity in Vanderbeke are not equivalent to the separate hydrolysis steps disclosed in the present invention. Vanderbeke does not teach or suggest the elements of claims 1-20. Furthermore Vanderbeke does not teach what is missing from Siren 1 and Siren 2" (page 9, 2nd paragraph).

This is not found persuasive. Siren 1 and 2 already teach the core invention. Vanderbeke et al was brought in since Vanderbeke et al teach using acid phosphatase with phatase to hydrolyze phytate, phytic acid, phytin or inositol phosphates. Since Vanderbeke et al teach the enzyme composition displays a higher synergetic phytate hydrolyzing efficiency. It would also have been *prima facie* obvious for one of ordinary skill in the art at the time the invention was made to treat the aqueous slurry at pH less than 4, since Vanderbeke et al teach preferably the treatment is carried out at a pH of about 2.5.

Applicant's arguments have been fully considered but they are not persuasive, and therefore the rejections in the record are maintained.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Qiuwen Mi whose telephone number is 571-272-5984. The examiner can normally be reached on 8 to 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

QM

/Michele Flood/

Primary Examiner, Art Unit 1655